UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/724,532	11/29/2003	Thomas D. Reed		3265

7590 07/29/2005

Thomas D. Reed, Ph.D.
1512 Northview Avenue
Cincinnati, OH 45223

EXAMINER	
CARLSON, KAREN C	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/724,532	REED, THOMAS D.	
	Examiner	Art Unit	
	Karen Cochrane Carlson, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-16 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-16 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.00

Claims 1-16 are currently pending and are under examination.

The claimed invention is found in SN 60/430,322. Therefore the priority date of the instant invention is December 12, 2002.

The disclosure is objected to because of the following informalities:

The number of the amino acids in SEQ ID NO: 1 is wrong. SEQ ID NO: 1 is a sequence comprising 30 amino acids. Thus, reference to amino acids L31, N34, F35, I38, L42, I48, V49, and L52, for example, cannot describe the amino acid positions within SEQ ID NO: 1. It is understood that SEQ ID NO: 1 is domain II of phospholamban and that the numbering is in reference to the 52 amino acid phospholamban sequence; however, discussion (and claiming) substitutions at position L52 has no basis in SEQ ID NO: 1.

At page 1, para. 2, the filing date of the provisional application is missing.

At page 1, line 29, "HMG" should be — HMW —.

Sequence identification numbers are missing at pages 9 and 10. It appears that Applicant must submit a new sequence listing and computer readable form (CRF) thereof in response to this Office Action.

The Examples are written in a prophetic manner rather than in the past tense as though the experiments were performed. Is this intended?

Appropriate correction is required.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-16 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claimed polypeptide and nucleic acid is not stated to be isolated or purified, thus reading on the product in nature.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 and 10-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The number of the amino acids in SEQ ID NO: 1 is wrong. SEQ ID NO: 1 is a sequence comprising 30 amino acids. Thus, reference to amino acids L31, N34, F35, I38, L42, I48, V49, and L52, for example, cannot describe the amino acid positions within SEQ ID NO: 1. It is understood that SEQ ID NO: 1 is domain II of phospholamban and that the numbering is in reference to the 52 amino acid phospholamban sequence; however, discussion (and claiming) substitutions at position L52 has no basis in SEQ ID NO: 1.

In Claim 1, it is confusing what is meant by "A polypeptide sequence comprising..." when it appears that what it intended is "An isolated polypeptide comprising the amino acid sequence of ..."

Claim 10 depends from Claim 7, and it appears that Claim 10 should depend from Claim 8 because Claim 7 and 10 are virtual repeats of each other. For examination purposes, Claim 10 has been take to depend from Claim 8.

In Claim 15, SEQ ID NO: 4 and NO: 6 are antisense strands. Therefore, Linking a second nucleotide sequence encoding a protein targeted to a sacro(endo)plasmic region to an antisense that does not encode a polypeptide would not result in targeting a protein targeted to a sacro(endo)plasmic region.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5, 6, and 11-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for PLN comprising Leu31Ala, Asn34Ala, Phe35Ala, Ile38Ala, Leu42Ala, Ile48Ala, Val49Ala, and/or Leu52Ala, does not reasonably provide enablement for any amino acid substitution other than Ala to be substituted at these amino acid positions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Kimura et al. (1997; J. Biol. Chem. 272(24): 15061-15064) show that the Val49Ala mutation resulted in loss of function for PLN (Table 1 and page 15063, para. 2). Haghighi et al. (2001; J. Biol. Chem. 276(26): 24145-24152) show that Val49Gly mutation resulted in gain of function (super inhibitor) for PLN (abstract; page 24145, right col, bottom through page 24146; page 24151, left col, para. 1). Thus, the particular amino acid substitution appears to determine the activity of the PLN.

In *Ex parte Forman* (230 USPQ 546) the Board considered the issue of enablement in molecular biology. The Board held that the following factors should be considered to determine whether the claimed invention would require of the skilled artisan undue experimentation:

1) Quantity of experimentation necessary: The activity of each mutant would have to be determined for each amino acids.

2) Amount of direction or guidance presented and 3) Presence or absence of working examples:: The specification teaches how to mutate PLN and to determine its activity but the

specification does not indicate that different amino acid substitutions would dramatically change PLN activity as shown in Kimura et al. and Haghighi et al.

4) Nature of the invention; 5) State of the prior art; 6) Relative skill of those in the art and 7) Predictability or unpredictability of the art: The invention involves biotechnology and recombinant techniques and those working in this art are highly skilled. The state of the prior art of Kimura et al. and Haghighi et al. show that this particular protein PLN is highly conserved and that substation of amino acids even with like amino acids such as Ala or Gly may/will change the activity of PLN.

8) Breadth of the claims: In general, the instant claims would not be viewed as particular broad. However, as determined by the prior art of record, the instant claims are too broad for the disclosure.

For all of these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Kimura et al. (1997; J. Biol. Chem. 272(24): 15061-15064).

As noted in the instant specification at page 4, Kimura et al. mutated each phospholamban (PLN) transmembrane (domain II) amino acids Leu31-Leu52, to Ala. (page 15062, left col.). Leu31Ala, Asn34Ala, Phe35Ala, Ile38Ala, Leu42Ala, Ile48Ala, Val49Ala, and

Leu52Ala mutations resulted in loss of function for PLN (Table 1 and page 15063, para. 2). Thus, Claims 1-3 are anticipated by Kimura et al.

Kimura et al. expressed these mutated PLN transmembrane domain amino acids from HEK-293 cells. Therefore, Kimura et al. were in possession of the nucleic acid encoding these mutant PLNs (Claims 11-13).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5, 6, 11, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Kimura et al. (1997; J. Biol. Chem. 272(24): 15061-15064) and Kimura et al. (1996; J. Biol. Chem. 271(36): 21726-21731).

The teachings of Kimura et al. (1997) are set forth above. Kimura et al. do not teach fusion proteins of the PLN mutants.

Kimura et al. (1996) teach that they could not assess the expression level of the Met-PLN^{28-52} because there is no antibody against domain II of PLN. Therefore, Kimura et al. (1996) added epitope tags Myc, FLAG, or HA to the PLN^{28-52} so that the fusion protein could be isolated using antibodies against Myc, FLAG, or HA (Page 21727, right col. para. 1).

It would have been obvious to a person having ordinary skill in the art to add epitope tags Myc, FLAG, or HA to the mutants of Kimura et al. (1997) so that the fusion protein could be isolated using antibodies against Myc, FLAG, or HA as demonstrated by Kimura et al. (1996) using fusion proteins of epitope tags Myc, FLAG, or HA to the PLN^{28-52}. Thus, linkage of the PLN mutants to a compound or macromolecule is obvious as applied to Claims 5, 6, and 14.

Claims 1, 4, 8, and 15 (SEQ ID NO: 3, 5) are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Kimura et al. (1997; J. Biol. Chem. 272(24): 15061-15064).

The teachings of Kimura et al. (1997) are set forth above. Kimura et al. do not teach fusion proteins of the PLN mutants. Additionally, Kimura et al. teach PLN double mutants comprising Asn34Ala/Ile48Ala or Phe35Ala/Leu44Ala. Kimura et al. demonstrated that the loss of function mutations dominated over the gain of function mutations to result in an inactive PLN.

It would have been obvious to one having ordinary skill in the art that the placement of two loss of function mutations such as Leu31Ala and Asn34Ala would result in an inactive PLN because Kimura et al. teach that each individual mutation results in loss of function and therefore double mutations comprising the individual mutations would also be predicted to result in a loss of function PLN. Evidence that the combination of two mutations resulting in the loss of function in PLN is in the dominance of the loss of function mutants in the double mutants comprising Asn34Ala/Ile48Ala or Phe35Ala/Leu44Ala as shown by Kimura et al. Claim 15 is included in this rejection because the nucleic acid encoding the mutant PLN is obvious over the mutant.

Claims 7, 9, 10, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Kimura et al. (1997; J. Biol. Chem. 272(24): 15061-15064) as applied to Claims 1, 4, 8, and 15 above, in view of Kimura et al. (1996; J. Biol. Chem. 271(36): 21726-21731).

The teachings of Kimura et al. (1997) are set forth above.

Kimura et al. (1996) teach that they could not assess the expression level of the Met-PLN^{28-52} because there is no antibody against domain II of PLN. Therefore, Kimura et al. (1996)

added epitope tags Myc, FLAG, or HA to the PLN^{28-52} so that the fusion protein could be isolated using antibodies against Myc, FLAG, or HA (Page 21727, right col. para. 1).

It would have been obvious to a person having ordinary skill in the art to add epitope tags Myc, FLAG, or HA to the loss of function double mutants of Kimura et al. (1997) so that the fusion protein could be isolated using antibodies against Myc, FLAG, or HA as demonstrated by Kimura et al. (1996) using fusion proteins of epitope tags Myc, FLAG, or HA to the PLN^{28-52}. Thus, linkage of the PLN mutants to a compound or macromolecule is obvious as applied to Claims 7, 9, and 10.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 571-272-0946. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen Cochrane Carlson PhD

***

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER